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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/618,868	07/14/2003	Bjorn M. Nilsson	13425-056002	6954

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EXAMINER	
BALASUBRAMANIAN, VENKATARAMAN	
ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 07/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/618,868	NILSSON, BJORN M.	
	Examiner	Art Unit	
	Venkataraman Balasubramanian	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 May 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-10,13-22 and 25-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-10,13-22 and 25-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/15/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' response, which included cancellation of claims 4, 11, 12, 23 and 24, addition of new claims 26 & 27 and amendment to claims 1, 9, and 13-22, filed on 5/15/2006, is made of record. Claims 1-3, 5-10, 13-22 and 25-27 are now pending, of which claims 2 and 3 were withdrawn from consideration in the previous office action. Claims 1, 5-10, 13-22 and 25-27 are under examination.

In view of applicants' response, all 112 second paragraph rejections except rejection of claim 22, made in the previous office action have been obviated. However, the following rejections made in the previous office action are maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 22 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the conversion steps a and b. the actual reactants are omitted rendering the claim a cryptic claim. Note reacting with chemical reagents wouldn't lead to desired product. This rejection is same as made in the previous office action.

Applicants' traversal is not persuasive. Note R_1 and R_2 includes alkyl, alkenyl, akynyl, aryl , heteroaryl etc. It is not clear how these radicals are derived and how would they react with Hal.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15, 16,18, 20 and 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of obesity, eating disorder, anxiety, depression, epilepsy, pain and schizophrenia embraced, does not reasonably provide enablement for treatment of any or all mood disorders, memory disorders, any or all sexual dysfunctions, and any or all urinary disorders embraced in these claim language. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant claims 15, 16,18, 20 and 26 are drawn to treatment of any or all mood disorders, memory disorders, any or all sexual dysfunctions, and any or all urinary disorders based on the mode of action of the instant compounds on serotonin receptor 5-HT_{2c} activity.

Instant claims are reach through claims. Reach through claims , in general have a format drawn to mechanistic, receptor binding or enzymatic functionality and thereby reach through any or all diseases, disorders or conditions for which they lack written description and enabling disclosure in the specification. In the instant case, because of the interaction of the compound formula I with serotonin receptor, it is recited that instant compounds are useful for treatment of above said any or all medical conditions for which there is no adequate written description and enabling disclosure in the instant

specification. The scope of the claims includes any or all medical condition due to serotonin receptor inhibition including those yet to be discovered as due said mode of action for which there is no enabling disclosure. In addition, the scope of these claims includes treatment of various medical conditions which are not adequately enabled solely based on the activity of the compounds provided in the specification. The instant compounds are disclosed to have serotonin receptor inhibitory activity and it is recited that the instant compounds are therefore useful in treating any or all medical conditions stated above for which applicants provide no competent evidence. It appears that the applicants are asserting that the embraced compounds because of their mode action as serotonin receptor inhibitor that would be useful for all sorts of medical conditions. However, the applicants have not provided any competent evidence that the instantly disclosed tests are highly predictive for all the uses disclosed and embraced by the claim language for the intended host. Moreover many if not most of neurological diseases. are very difficult to treat or to prevent and despite the fact that there are many drugs with the same mode of action.

The scope of the claims involves thousands of compounds of claim 1 as well as the thousand of diseases embraced by the term medical condition

No compound has ever been found to treat and prevent all types of medical conditions generally. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The existence of such a "compound" is contrary to our present understanding of modern medicine. Thus, it is beyond the skill of clinician today to get an agent to be effective against cancers

generally. Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided. See Ex parte Jovanovics, 211 USPQ 907, 909; In re Langer 183 USPQ 288. Also note Hoffman v. Klaus 9 USPQ 2d 1657 and Ex parte Powers 220 USPQ 925 regarding type of testing needed to support in vivo uses.

Next, applicant's attention is drawn to the Revised Interim Utility and Written Description Guidelines, at 66 FR 1092-1099, 2001, wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed method of prophylaxis solely based on the agonist activity disclosed for the compounds. The state of the art is indicative of the requirement for undue experimentation. See non-patent literature provided in the Information Disclosure Statement.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Therapeutic use of the compounds in serotonin related medical condition that require 5-HT_{2c} agonist activity.

2) The state of the prior art: The publications cited in the Information Disclosure Statement expressed, at the time of the instant invention was made, that treatment of medical conditions mediated by serotonin by 5-HT_{2c} agonist activity i is still exploratory.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use for treating any or all condition of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: Specification has no working examples to show treating any or all condition and the state of the art is that the effects of inhibiting 5-HT_{2c} activity are unpredictable and at best limited to treatment of obesity.

6) The breadth of the claims: The instant claims embrace any or all condition including those yet to be related to 5-HT_{2c} activity.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical

nature of the invention, the unpredictability of receptor-ligand interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards treating the variety of diseases of the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

This rejection is same as made in the previous office action but now limited to claims 15, 16, 18, 20 and 26.

Applicants' traversal to overcome this rejection is not persuasive. Applicants have provided support for specific disorders which are on that basis are deemed a enabled. However, instant claims still include several generic disorders such mood disorders, memory disorders, sexual dysfunction for which there appears to be no enablement or objective enablement in the literature references provided by the applicants. In addition, it is not clear how blocking plaque formation would lead to treating memory disorder as in Alzheimer's disease. There appears to be no support for treating all substance abuse.

Hence, this rejection as applied to the above mentioned claims, is proper and is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 5-10, 13-22 and 25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baroni et al. 0580465.

Baroni et al. teaches several heterocyclyl piperazine compounds useful as %-HT3 agonists, which include instant compounds. See entire documents, especially page, formula I and note the definition of, X, Y, R, R_1 and R_2 overlap with instant variable groups. Note when $R_{2\ is}$ halogen, the compounds taught by Baroni et al. include instant compounds. Note the process of making is same as recited instant claim 22

See pages 4-5 for examples 1-3 which show a pyridine analog.

Instant claims require a pyrimidine core while Baroni et al exemplifies only pyridine core. However, Baroni et al clearly teaches equivalency of the exemplified pyridine compounds with those of pyrimidine compounds generically claimed for compound of formula I. See page 2 and note Y can be N and with X as CH.

Thus it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make compounds variously substituted piperazinyl-pyrimidines including those generically taught as permitted by the reference and expect resulting compounds (instant compounds) to possess the uses taught by the art in view of the equivalency teaching outline above.

This rejection is same as made in the previous office action. Applicants' argument to overcome this rejection is not persuasive.

First of all, Baroni's X and Y varible definition clearly includes pyridine, pyrimidine and pyrazine which are same as instant cores embraced in instant X, Z and Y definition. Baroni et al., clearly states these three choices in column 1, line 59.

Secondly, Baroni et al., also points out in column 1, paragraph 1, usefulness of both piperazine bearing pyridine and piperazine bearing pyrimidine as having 5-HT_3 receptor activity.

Applicants' also have argued that the teachings of Baroni is similar to In re Baird 29 USPQ 2d 1550, 1552-1553 and In re Jones 21 USPQ 2d 1941, 1943 (fed Cir. 1992). Both In re Baird and In re Jones are not to the point.

In re Baird, court held that there is no guidance provided to select a specific variable group. In the instant case, Baroni et al., teaches , as noted above, both pyridine

and pyrimidine core compounds are equivalent as far as the 5-HT_3 receptor activity. Thus, providing guidance to select pyrimidine core based on the pyridine compounds exemplified.

Hence, this rejection is proper and is maintained.

Election/Restrictions

This application contains claims 2 and 3 are drawn to an invention nonelected with traverse in Paper dated 9/6/2005. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571)

272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson whose telephone number is (571) 272-0661.

The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

Venkataraman Balasubramanian

7/24/2006